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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/876,767	06/07/2001	Mamoru Uchiyama	PC9980ACJG	8873

7590 01/26/2005

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EXAMINER

ZHOU, SHUBO

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 01/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/876,767	Applicant(s) UCHIYAMA ET AL.	
	Examiner Shubo (Joe) Zhou	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 September 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-7 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 17 September 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|-----------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>12/8/03, 9/17/04</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Amendments

1. Applicants' response to the previous Office action and amendment, filed 9/17/04, is acknowledged. The amendments are entered.

Claims 1-7 are currently pending and under consideration.

Applicant's arguments in response to the previous Office action have been fully considered. The following rejections and/or objections are reiterated from the previous Office action, mailed 10/2/03, and constitute the complete set presently being applied to the instant application. Rejections and/or objections not reiterated from previous Office actions are hereby withdrawn.

Specification

2. The amendment to the specification adding a program listing with the file name "2dfp_abs.spl" filed 7/14/04 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

While the term "2dfp_abs.spl" is disclosed in the original disclosure, the detailed program list was never presented. The detailed program is thus considered as new matter.

Applicant is required to cancel the new matter in the reply to this Office Action.

Note that since the compact discs filed on 7/14/04 also contain the program list of 2dfp.spl, upon cancellation of the code of "2dfp_abs.spl", applicants are requested to file new compact discs containing only the codes of 2dfp.spl in compliance with 37 CFR 1.52.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. Claims 1-2, and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hurst et al. (WO 98/07107, 19 Feb. 1998) in view of Niwa, T. (IDS document: Predicting of Drug Absorption using Neural Network. Symposium on Structure-activity Relationships. Japan, Nov. 10, 1999).

The claims are drawn to a method of predicting pharmacokinetic properties of a molecule comprising preparing 2-D structures of molecules in a training set, constructing a 2-D fingerprint

by counting the number of structural descriptors consisting of predefined 20-80 atoms/fragments or substructures, analyzing the 2-D fingerprint with a statistical method to yield a QSPR model, and using the model to calculate the pharmacokinetic property of a trial molecule.

Hurst et al. disclose a method of using 2-D fingerprints and such statistical methods as partial least squares to build QSPR models for a series of molecules to predict their chemical activity. See page 1, "Technical Field", and page 6. The 2-D fingerprint is built with structural descriptors of fragments of different numbers depending on the size and structures of molecules.

Hurst et al. do not explicitly disclose using the method for predicting pharmacokinetic property absorption of a molecule. Hurst et al. do not explicitly set the number of structural descriptors as 20-80 atoms/fragments or substructures. However, Hurst et al. disclose that this can be done using SYBYL, such as Sybyl line notation.

Niwa teach of using neural network and 2-D fingerprints to predict human intestinal absorption of drugs. Different structural descriptors are used for the analysis. See table on page 3. Niwa concludes that the prediction using the 2-D method generate equivalent good results with absorption as compared to 3-D methods, and is especially suitable to predict the absorption of a lot of compounds. See pages 3-4.

One of ordinary skill in the art would have been motivated by Niwa to modify the method of Hurst et al. to use the 2-D fingerprints and statistical model to predict the absorption property of a drug because Niwa particularly states that this method is especially suitable to predict the absorption of a lot of compounds. See pages 3-4. While Hurst et al. do not explicitly recite 20-80 atoms/fragments or substructures as structural descriptors, they teach that the number of atoms can be as low as two, and with a maximum number equal to the number of atoms in the molecule. Thus, it would have been obvious to one of ordinary skill in the art that the number of atoms/fragments used as structural descriptors would be variable depending on the length of the molecules. As to the internally developed macro used to construct the 2-D fingerprints of

structural descriptors in the claims, , and that this could equally well be done using any other means, which would be standard and well known to those in the art. It is noted that the internally developed macro of the instant claims is also written with SYBYL. Thus, different programs written with the same language SYBYL would have been obvious to one of ordinary skill in the art.

6. Claims 3-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hurst et al. (WO 98/07107, 19 Feb. 1998) in view of Niwa, T. (IDS document: Predicting of Drug Absorption using Neural Network. Symposium on Structure-activity Relationships. Japan, Nov. 10, 1999), as applied to claims 1-2, and 7 above, further in view of Markin et al. (IDS document: Pharmaceutical Research, Vol. 5, pages 201-208, 1988.

The claims drawn to a method of predicting such pharmacokinetic properties as distribution, metabolism, or excretion of a molecule.

As applied to claims 1-2, and 7 above, Hurst et al. disclose a method of using 2-D fingerprints and such statistical methods as partial least squares to build QSPR models for a series of molecules to predict their chemical activity. See page 1, "Technical Field", and page 6. The 2-D fingerprint is built with structural descriptors of fragments of different numbers depending on the size and structures of molecules.

Niwa teach of using neural network and 2-D fingerprints to predict human intestinal absorption of drugs.

Hurst et al. in view of Niwa as applied to claims 1-2 and 7 above, do not show using the 2-D fingerprint modeling for predicting such pharmacokinetic properties as distribution, metabolism, or excretion of a molecule.

Markin et al. disclose a method of using graph theoretical approach to build a quantitative structure activity model for benzodiazepines for predicting its pharmacokinetic properties including distribution, metabolism and excretion. Markin et al. conclude that the quantitative structure activity model works for all the pharmacokinetic properties. See page 201, Abstract.

It would have been obvious for one of ordinary skill in the art to modify the method of Hurst et al. in view of Niwa as applied to claims 1-2 and 7 above, to use the 2-D fingerprint method for predicting other pharmacokinetic properties: distribution, metabolism and excretion because Markin et al. successfully predicted all these pharmacokinetic properties including absorption, distribution, metabolism and excretion for drug benzodiazepines.

Conclusion

7. No claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shubo (Joe) Zhou, whose telephone number is 571-272-0724. The examiner can normally be reached Monday-Friday from 8 A.M. to 4 P.M. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph.D., can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Patent Analyst Tina Plunkett whose phone number is (571) 272-0549.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is

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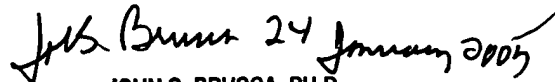
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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Shubo (Joe) Zhou, Ph.D.



Patent Examiner

JOHN S. BRUSCA, PH.D.
PRIMARY EXAMINER